A STUDY ON MATHEMATICAL MODELLING AND SIMULATION OF BIOHEAT TRANSFER IN TISSUE

SYNOPSIS

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in the partial fulfillment for the degree of

Doctor of Philosophy
in
Mathematics

By

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1 Title

A STUDY ON MATHEMATICAL MODELLING AND SIMULATION OF BIOHEAT TRANSFER IN TISSUE.

2 Introduction

The largest organ of the body is skin and surface area of skin is 1.5 - 2 m^2 and takes approximately 16% of the humans body weight. It perform many functions including keep safe us from microorganisms, bacteria and virus, helps to regulate body temperature, and helps to feel the sensations of touch, heat, and cold. Kolarsick et al. (2011) There are seven layers of the skin, which are as follows with their functions:

- Stratum Corneum: It is made up of dead skin cells which is known as keratinocytes. It is like a barrier which keeps bacteria away and contain moisture.
- Epidermis: This layer of skin produce a water-resistant barrier and creates our skin color.
- Dermis: It is the surface of skin below the epidermis. It carry connective tissue and sweat glands.
- Subcutaneous: The surface of the skin under Dermis is the deeper subcutaneous tissue, which is form of fat and connective tissue.
- Hypodermis: It contain fat cells which gives softness to the skin.
- Muscles: Muscles give moments and volume to the body.
- Bone: Bones cells are continuously dying and again restored known as bone metabolism.

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There are many diseases in the world. Diseases describe itself as disorder and announces its presence in the form of symptoms.

Cancer is a group of diseases in which abnormal cells divide uncontrollably and grow to other parts of the body (Challa and Mohammad, 2011). It is major leading cause of death in human life. If the spread of abnormal cells is not controlled, it can result in death. Nowadays million of people have been died by tumor and cancer. So that the treatment of cancer is required. Several researchers are doing work for tumorous and cancerous treatment with high accuracy through different therapies such as hyperthermia, diathermia, thermal abelation. There are 62 cancer centers in India. Some of which are Tata Memorial hospital (Mumbai), Cancer care foundation of India (Mumbai), Tata Memorial hospital (Kolkata), Rajiv Gandhi cancer institute and research centre (Delhi) etc.

There are 345 national and international cancer organizations . From which there are only 4 in India which are

- Associations of Gynecologic Oncologist of India. (Maharashtra)
- Associations of Radiation Oncologist of India. (West Bengal)
- Indian Cancer Society. (New Delhi)
- Indian Cooperative Oncology Network. (Ahmedabad)

Mathematical modelling of thermal therapy is depend on transfer of heat in biological things. In 1822, a French scientist Joseph Baptiste Fourier introduced his most famous work which is also called the law of heat conduction. This heat conduction law is commonly known as Fourier law of heat conduction. In this law, heat flux based on cross section area A of material and temperature gradient (∇T) i.e.

$$q(x,t) \propto -A\nabla T(x,t),$$

$$i.e.\ \ q(x,t) = -kA\nabla T(x,t),$$

where $q(x,t)$ heat flux, k is proportionality constant which is known as thermal conductivity of material and ∇T is temperature gradient. Negative sign denotes as temperature decreases as distance increases. If $A = 1$ then $q(x,t)$ is heat flux par unit area i.e. heat flux density, which is given as:

$$q(x,t) = -k\nabla T(x,t). \tag{1}$$

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Non-Fourier heat conduction law is next modification of Fourier's law of heat conduction in sense of finite speed propagation of thermal wave. There are two types of constitutive relation which is formulated under non-Fourier law of heat conduction.

Then Cattaneo (1958) and Vernotte (1958) separately gave a fundamental connection between heat flux and temperature gradient by presenting a relaxation time due to heat flux which is given as

$$q(x, t + \tau_q) = -k\nabla T(x, t), \tag{2}$$

which is known as the single-phase-lag (SPL) constitutive relation.

Further, Tzou (1996) suggested a dual-phase-lag (DPL) constitutive relation involving two kinds of lag time because of heat flux and temperature gradient respectively which is next modification of SPL constitutive relation, i.e.

$$q(x, t + \tau_q) = -k\nabla T(x, t + \tau_T),$$

where τ_q & τ_T are lag time because of heat flux and temperature gradient, respectively.

There are many areas of heat transfer like mechanical engineering, thermal plant, biomedical, bio-engineering. Our interest of study in the area of bioheat transfer. So that we described about bioheat transfer process in the following section.

2.1 Bioheat Transfer

Bioheat transfer is the study of transport of thermal energy from one part to another part of the body internally. Heat transfer which is involving in biological system, is known as bioheat transfer. It plays a vital role in field of biomedical, bioengineering, mainly thermal therapy, etc. Heat transfer is very composite procedure in living biological tissue (Kumar et al., 2015). It has multiple mechanisms which includes conduction in tissues, convection between blood and tissues, blood perfusion through micro-vascular cells, external heat generation and metabolic heat generation (Afrin et al., 2011). Therefore, the one dimensional energy balance equation which is given as: (Kumar et al. , 2016)

$$\rho c \frac{\partial T(x,t)}{\partial t} = -\nabla q(x,t) + Q_b + Q_m + Q_r \tag{3}$$

where ρ, c are density and specific heat of material. Q_b, Q_m and Q_r are blood perfusion rate, metabolic heat generation and external heat generation in living things, respectively.

The study of effects of temperature alterations on biochemical rate processes has been divided into

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two general categories: thermal therapy and cryobiology (subfreezing temperature). The study of our interest is in thermal therapy which is described in following section.

2.2 Thermal therapy

Thermal therapy is the transfer of heat energy into or out of the body. Thermal therapy is the use of heat in therapy and electromagnetic energy, ultrasonic waves, and other thermal-conduction-based devices are used as heating sources. Heat transfer has many medicinal applications which includes either increasing or decreasing of temperature (Diller et al. , 1992). It is divided into three different categories based on temperature level and time duration (Habash et al. (2006)) i.e.

- Diathermia: The temperature of the part of the body heating upto 41° C for 6-72 hours.
- Hyperthermia: In hyperthermia, the temperature of body increased upto 41-45°C for 15-60 minutes. Hyperthermia is used for a cancer treatment in oncology.
- Thermal ablation: Thermal ablation which is also known as high-temperature hyperthermia with temperature > 50°C for 4-6 minutes is used to kill the cancerous cells. It is used to kill the whole tumor without damaging the whole body structure.

3 Expected new knowledge

Objectives of our research work are given as follows:

1. Proposed study of non-linear dual-phase-lag model for heat transfer in tissue with periodic boundary condition.
2. Proposed study of non-linear dual-phase-lag model for different temperature dependent blood perfusion rate.
3. Proposed study of TPL model for heat transfer in tissue.
4. Proposed study of heat transfer in tissue for hyperthermia.

4 Literature review

Askarizadeh et al. (2014) studied temperature distribution in skin during transient heat source in dual-phase-lag model of bio-heat transfer.

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Diller et al. (1998) studied the factors that analyzed the heat transfer in living systems. They also studied the application in fundamental research and in clinical diagnosis treatment.

Habash et al. (2006) explained development in thermal therapy with three techniques , one is hyperthermia with temperature 40-41°C for 6-72 hr, second is moderate-temperature hyperthermia with temperature 42-45°C for 15-60 min and third is thermal ablation which is also known as high-temperature hyperthermia with temperature > 50°C for 4-6 min. They also discussed the biological and mechanisms effects of heat.

Jiang et al. (2012) using expansion of Taylor's series and modified Riemann-Liouville fractional derivatives to proposed a new fractional thermal wave model of the bioheat transfer. In the finite medium they also obtained the fractional thermal wave model of the bioheat transfer in a one-dimensional analytical solution. Numerical results were graphically presented for many values of distinct parameters.

Kengne et al. (2014) observed the one-dimensional bio-heat transfer equation with quadratic temperature dependent blood perfusion, which control the temperature distribution in biological tissues. They also found the exact analytical thermal traveling wave solution using an extended mapping method with symbolic computation, which also describe the non-uniform temperature distribution inside the bodies. They found the exact solution which is also used to obtained the temperature distribution in the tissues. It is also observed that increased perfusion causes a decline in local temperature.

Kumar et al. (2015) studied the temperature distribution in a finite living tissue in existance of metabolic and external heat source. The comparison of analytical results obtained from three models i.e. Classical model, single-phase-lag model and dual-phase-lag model for bioheat transfer for biological tissue using Laplace transfer tissue. The results obtained from three models then differentiate with experimental data of (Stolwijk et al., 1996) and observed that from three models, dual-phase-lag model gives better result.

Kumar et al. (2016) studied for bi-layer tissue that DPLBHT model is solved by using finite element Legendre wavelet Galerkin method with Fourier and non-Fourier boundary conditions. They observed that in spherical symmetric coordinate system moderate hyperthermia temperature with range 41-46°C could be better achieved. The effect of phase-lag times only in tumor region and considered the effect of variability of magnetic heat source parameters is also shown. The features of these parameters during magnetic fluid hyperthermia treatment has been described in detail.

Kumar et al. (2016) examined that during thermal therapy, the thermal behavior in living biological tissue with DPLBHT model with different non-Fourier boundary conditions and various coordinate systems. The properties of Legendre wavelets is used for the analytical solution of the

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problem with the finite difference method. They conclude that healthy tissue are less affected when second and third kind of boundary condition used with spherical symmetric coordinate system.

Kumar et al. (2017) used non-linear DPLBHT model to deals with numerical modeling and solution of heat transfer in skin tissues. To predicts more accurate results they assumed the blood perfusion as temperature-dependent which converted in non-linear DPLBHT model. For the solution of non-linear problem, they used the hybrid numerical methods which include finite difference and Runge-Kutta (4,5) method. They also observed that due to absence of phase-lag phenomena in Pennes bioheat transfer model, quickly get steady state and measure higher temperature than thermal and dual-phase-lag non-linear models.

Kumar et al. (2018) studied the mathematical modelling and simulation of heat transfer under Dirichlet boundary condition. For the therapy of tumorous cells, they used the non-linear DPLBHT model. To solve the non-linear problem they used a hybrid numerical method combine two program, first is finite difference and second is Runge-Kutta (4, 5) schemes. In particular cases they obtained the exact solution. They obtained the non-linear DPLBHT model was closed to experimental data when they differentiate the non-linear dual-phase-lag bioheat transfer model, non-linear single-phase-lag bioheat transfer model and non-linear Pennes bioheat transfer model with experimental data, when the difference of blood perfusion rate and metabolism was real function of temperature in same situation. They also shows the effect of coefficient of blood perfusion rate, relaxation and thermalisation time, dimensionless heating source parameters on dimensionless temperature distribution.

Oke et al. (2018) discussed a mathematical model of breast cancer in the presence of chemotherapy treatment and ketogenic diet governed by a system of ordinary differential equations. Also, In the absence of anti-cancer drugs, ketogenic diet, they established sufficient conditions on parameter values to ensure cancer persistence and cancer emission when anti-cancer drugs, immune-booster, and ketogenic diet were included. To decrease the number of cancerous cells, they used the optimal control theory.

Okajima et al. (2009) gave the derivation and application of the general characteristics of bioheat transfer for medical applications. From solutions of one-dimensional Pennes' bioheat transfer equation, two general bioheat transfer characteristics were also derived. All results gave details on temperature distribution in biological tissue for different thermal therapies.

Zhang et al. (2014) When blood perfusion rate varies linearly, quadratically or exponentially with temperature under steady state condition using Pennes bioheat transfer model has been solved using boundary reciprocity method

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5 Methodology

In this research work, different numerical methods will be used in the solution of problems. The proposed numerical methods are

- Wavelet Collocation method
- Wavelet Galerkin method
- Finite difference method
- Runge-Kutta-Fehlberg (4,5) method

In particular cases problem will be solved by analytical method.

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6 Publications

- **Neha Sharma**, Surjan Singh and Dinesh Kumar (2021), 'Numerical solution of nonlinear dual-phase-lag model for analyzing heat transfer in tissue during thermal therapy' *Computational and Mathematical methods, John Wiley and Sons Ltd.*, DOI: https://doi.org/10.1002/cnm4.1183 **Published**.

- **Neha Sharma**, Surjan Singh, Dinesh Kumar and Parvinder Kaur 'Solution of non-linear DPL model for temperature dependent blood perfusion rate' *International Journal of Nonlinear Analysis and Applications*, **Under Review**.

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We have critically examined the synopsis of Thesis/Dissertation Problem entitled :**A STUDY ON MATHEMATICAL MODELLING AND SIMULATION OF BIOHEAT TRANSFER IN TISSUE** submitted by : **Ms. Neha Sharma,** Registration No :**BS18PSMA002** for M.Sc/M. Tech/Ph.D degree in the subject of: **Mathematics** to the Akal College of Basic Sciences of the Eternal University, Baru Sahib(HP). It is certified that the research problem in original; programme of work is properly planned, feasible to carry out and is of good academic and practical significance.

Ms/Mr.: **Ms. Neha Sharma** gave a presentation on the above mentioned research problem to the Research Degree Committee and other faculty members and students on **August 13, 2021** and his/her performance is Satisfactory/Unsatisfactory. Satisfactory

Synopsis is recommended for acceptance in by the Eternal University.

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